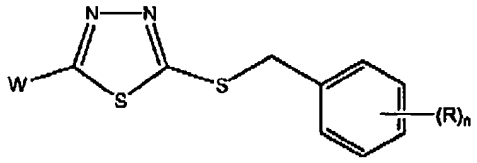
CLAIM AMENDMENTS

10. – 28. (canceled)

29. (new) A method of treating a disease selected from the group consisting of psychoses, pain, epilepsy, neurodegenerative diseases, stroke, head trauma, multiple sclerosis, spasticity and myoclonus by administering a therapeutically effective amount of a compound of the formula:



where:
n is 0, 1, or 2;
each R is chlorine; and
W is aryl or heteroaryl,
or a pharmaceutically acceptable salt thereof.

30. (new) The method of Claim 29 where the compound is selected from
2-[(2,6-dichlorophenyl)methylthio]-5-(pyrazin-2-yl)-1,3,4-thiadiazole,
2-(benzylthio)-5-phenyl-1,3,4-thiadiazole,
2-(benzylthio)-5-(pyridin-3-yl)-1,3,4-thiadiazole,
2-[(2,6-dichlorophenyl)methylthio]-5-phenyl-1,3,4-thiadiazole, and
2-(benzylthio)-5-(pyrazin-2-yl)-1,3,4-thiadiazole.

The Examiner then stated that "Claims 1-9 are drawn to a method of treating a disease state treatable by the inhibition of the glycine transporter 2. The specification reads on any and all disorders such as [the list in claim 29], etc." The Examiner then refers to the article by Gomeza et al., *Current Opinion in Drug Discovery and Development*, 2003 on glycine transporter isoforms. He quotes the article at page 680 (the Conclusions):

> GlyTs have only recently emerged as potential sites of drug action in disorders caused by deficits in inhibitory glycinergic or excitatory NMDA receptor-mediated neurotransmission. In particular, GlyT-1 antagonists appear to have great promise for the treatment of schizophrenia, a widespread psychiatric disease for which no effective medication is currently available. In addition, selective antagonists for GlyT-2 should be useful as novel antispastic and muscle-relaxant and, in particular, analgesic compounds that have little effect on higher brain circuits. Efforts to <u>further advance</u> GlyT pharmacology thus appear highly warranted. [Emphasis by Examiner]

and then asserts that "The above quote makes it clear that, at least as of 2003, which is a year later than the filing of this application, much more than routine experimentation would be required to find a way to use GlyT2 antagonists to treat pain or spasticity. As of 2002, there was only the 'potential', and success would require future development, i.e. more than routine experimentation."

Applicants respectfully disagree. Claim 29 now limits the disease states treated not to any treatable by inhibition of GlyT2, but to a specified list of diseases, and the compounds to be used to a narrow Markush group for which the GlyT2 inhibitory activity of a member has been demonstrated.

Further, Applicants submit that the Gomeza et al. article does not have the significance asserted by the Examiner. Far from casting doubt on the utilities asserted in the application and claimed in claim 29, Gomeza et al. support them by stating explicitly, in the second last sentence that "selective antagonists for GlyT-2 should be useful as novel antispastic and muscle-relaxant and, in particular, analgesic compounds that have little effect on higher brain circuits", thereby emphasizing the value of the test for GlyT2 antagonism as predictive of pharmaceutical utility. The final sentence of the article suggesting that "further research on GlyT2 pharmacology is highly warranted" does not in any way cast doubt on what is known or suggest that more than routine experimentation would be required to develop a compound, instead it emphasizes the value of learning yet more.

The Examiner is referred to the "Background Art" section of US Published Application No. 2003/0216385 (Tobe et al.), the US equivalent of the Japanese-language PCT publication cited in the art rejections of prior claims 1-6. In that section, Tobe et al. discuss the glycine transporter and potential uses of glycine transporter inhibitors, with many references. For example, at paragraph [0006], lines 9-12, they say, citing Yaksh et al., *Pain*, 1989 (the same reference cited in this application at page 2, lines 13-15), that "It is suggested that the inhibition of GLYT2 induces the attenuation of pain transmission in the spinal cord ... ." thereby implying that a GlyT2 antagonist would be useful to treat pain.

Applicants respectfully submit that the specification provides all information needed for the person of ordinary skill in the art to practice the claims without undue experimentation, and that claims 29 and 30 are therefore enabled by the specification. Withdrawal of the rejection is requested.

The 35 USC 112, ¶2 rejection

Claims 1 and 5 were rejected under 35 USC 112, ¶2 for indefiniteness. This rejection is respectfully traversed as applied to claims 29 and 30.

The Examiner stated that "optionally substituted" was unclear as to the nature and number of substituents intended. Claims 29 and 30 do not contain the term "optionally substituted", and the rejection is believed moot.

The Examiner also stated that claim 1 "is of indefinite scope for more than one reason. First, no particular disorder is recited. Second, the claim language may read on diseases not yet fully understood to be affected by glycine transporter antagonists." New claim 29 recites a particular list of disorders, and therefore cannot read on diseases not yet fully understood to be affected by glycine transporter antagonists. Withdrawal of the rejection is requested.

The 35 USC 102(a) and (b) and 103(a) rejections

Each of claims 1-6 was rejected under 35 USC 102(a) or (b) and/or 103(a) over one or more of Tobe et al. (WO 01/87855), Chakravarty et al. (GB 2263635), and Gulerman et al. (*Il Farmaco*, 1997).

Applicants note that the Office Action in ¶6 referred to "Tobe et al. (US 5,506,347)" but this is believed to be a reference to Tobe et al. (WO 01/87855) because US 5,506,347 was not listed on the PTO-892 accompanying the Office Action and is any event a patent to Erion et al. on lyxofuranosyl analogues of adenosine completely irrelevant to the subject matter of this application.

However, none of claims 7-9 was so rejected; and because claims 29 and 30 correspond in compound scope to claims 7 and 8, the rejections are believed inapplicable to claims 29 and 30.

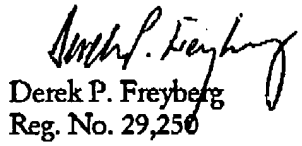
Applicants therefore submit that claims 29 and 30 are not anticipated by or unpatentable over any one of unpatentable over Tobe et al. (WO 01/87855), Chakravarty et al. (GB 2263635), and Gulerman et al. (*Il Farmaco*, 1997), and withdrawal of the rejection is requested.

Conclusion

For the reasons given above, Applicants submit that the claims are enabled under 35 USC 112, ¶1, definite under 35 USC 112, ¶2, and are not anticipated or unpatentable over the art cited. Re-examination and allowance of the claims are respectfully requested.

Applicants reserve the right to file divisional and/or continuation application(s) to the subject matter canceled in response to the restriction requirement or the present Office Action.

Respectfully submitted,



Derek P. Freyberg
Reg. No. 29,250

Telik, Inc.
3165 Porter Drive
Palo Alto CA 94304-1213
650.845.7720
20 August 2004